Effect of lofexidine versus diazepam on anxiety during opioid detoxification: finding from a randomized double-blind controlled trial

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Background
Lofexidine, an alpha-2 adrenergic receptor agonist, has been approved in the United Kingdom for the treatment of opioid withdrawal symptoms. Many research studies have demonstrated the efficacy and safety of lofexidine comparing with placebo, clonidine, methadone, buprenorphine. However none of these studies has compared lofexidine with diazepam in managing heroin withdrawal syndrome. This study looks at the efficacy of lofexidine versus diazepam on reducing anxiety symptoms during inpatient detoxification.

Method
This is a randomised double-blind investigator initiated trial in National Addictions Management Service (NAMS), Singapore. Maudsley Addiction Profile (MAP) containing measurements on the severity of anxious and depressed moods was assessed every 3 days after admission (on days 3, 6, 9 and 12) by the delegated researcher. Subjects received either standard treatment diazepam or the trial medication lofexidine up to 10 days followed by 4 days continuous psychological education during NAMS inpatient detoxification programme. Initial dosage of lofexidine and diazepam started from 0.8mg and 10 mg respectively, per day in divided doses. The peak dosage of lofexidine and diazepam were 2.2 mg and 15mg (on day 3, 4) respectively. The subjects in both groups subsequently received the tapering doses till day 10. CBT based Psychological intervention were provided throughout the whole study period.

Results
Total 111 patients with diagnosis of heroin dependence (DSM-IV-TR) were randomized to the trial, 56 in lofexidine group and 55 in diazepam group. The severity of anxiety symptoms in MAP such as "feeling tense", "suddenly scared for no reason", "feeling fearful", "nervousness of shakiness inside" and "spells of terror" or "panic" reduced in both treatment groups over time during the study period. There were no statistical differences comparing these anxiety symptoms between lofexidine group and diazepam groups.

Discussion
Diazepam is prescribed as the standard pharmacological treatment in the management of opioid withdrawal syndrome in NAMS. However, its addictive pharmacological profile limits its usage for opioid dependence. The results suggest that lofexidine, a non-opiate, non-addictive alpha-2-agonist could be an alternative medication in assisting opioid detoxification in Singapore.